

THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Menon
Serial No.: 09/521,442
For: METHOD OF TREATING SKIN CONDITIONS
Filed: March 7, 2000
Examiner: J. Venkat
Art Unit: 1615
Confirmation No.: 1007
Customer No.: 27,623

Attorney Docket No.: 680.0035USU

DECLARATION UNDER 37 C.F.R. 1.132

I, Peter M. Elias, M.D., declare the following:

I received a B.A. degree in biological sciences from Stanford University in 1963, an M.D. degree from the University of California at San Francisco in 1967, and an M.S. degree in experimental pathology from the University of California at San Francisco in 1975. I have practiced dermatology from 1974 to the present. I am currently a Professor of Dermatology and Vice-Chairman in the Department of Dermatology at the University of California at San Francisco. I have conducted research in dermatology and skin diseases since 1969. I have authored or co-authored at least 422 publications pertaining to skin biology and dermatology as listed in the attached Curriculum Vitae.

Cellulite is a cosmetically-disfiguring condition in which afflicted skin can look like orange peel. Cellulite is typically localized at the thighs, hips, or abdomen of women, although cellulite can also afflict males. The microscopic pathology of

cellulite takes the form of a localized proliferation of fibroblasts and adipocytes. Fibroblasts readily transform into adipocytes with appropriate hormonal/growth factor signaling. The process of fibroblast-to-adipocyte metamorphosis results in a gradual accumulation of adipocytes over time. As triglycerides accumulate in adipocytes, these cells hypertrophy and ultimately restrict venous and lymphatic drainage from affected sites.

I have reviewed the contents of the above-captioned application, including the pending claims and the working examples, and the Office Action mailed January 4, 2006 and understand them.

I disagree with the Examiner's assertion of lack of enablement for claims 36 to 51 in the Office Action. The disclosure of the above-captioned application clearly articulates the invention as set forth in the claims 36 to 51 and places me, a person skilled in the arts of skin biology and dermatology, in possession of it. Examples 1 and 2 of the above-captioned application clearly demonstrate the stabilizing effect of perilla oil on PPAR upregulation in the presence of known PPAR agonists. Page 1, lines 12 and 13 of the above-captioned application directly associates the treatment or amelioration of cellulite with the upregulation of PPAR and this association is logical and reasonable, particularly in view of my observations in the following paragraph.

I have also reviewed the Interview Summary appended to the Office Action. The Continuation of Substance of Interview appended to the Interview Summary states in the last two sentences that "The examiner informed [applicant] that there is

no nexus between cellulite and the prevention of upregulation of PPAR. Competent documentation establishing this nexus would be given careful consideration." I disagree with this conclusion, based upon many years of work with the PPAR family of activators, and their effects on cutaneous development, growth, differentiation, barrier function, and inflammation. I have over 30 publications during the past 10 years that focus on the effects of PPAR activators in skin biology. Therefore, I feel qualified to comment on this subject.

After reviewing the above-captioned application, including the examples, I believe there is a nexus between the formation of cellulite and the upregulation of PPARgamma.

PPARgamma receptors regulate adipocyte growth and differentiation. Hence, ligand activators (agonists) of PPARgamma receptors, such as ciglitazone, stimulate adipocyte growth. Because adipocytes are stimulated, i.e., up-regulated, they proliferate and hypertrophy in response to treatment with PPARgamma ligand agonists. It follows that blocking PPARgamma receptors would be a suitable means for treating or ameliorating cellulite. PPARgamma blocking can be achieved by two different mechanisms: 1) down-regulation of PPARgamma receptor levels, and 2) competitive inhibition with endogenous PPARgamma activators, such as leukotriene B4, thereby reducing (i.e., stabilizing) the numbers of PPARgamma receptors that are available to be activated.

The examples of the above-captioned application demonstrate that there is a reduction of PPRE activity when perilla oil is combined with G3, a known PPAR ligand agonist, as compared to the level of PPRE activity when G3 is tested alone. This decrease in PPRE activity indicates perilla oil is a stabilizer of PPAR,

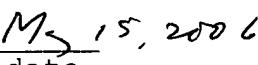
which is a legitimate mechanism to treat cellulite production and retention in a human.

I am not aware that PPARgamma stabilizers have been employed to treat cellulite in the skin biology or dermatology art outside of the disclosure in the above-captioned application. More specifically, I am not aware that perilla oil has been employed to treat or ameliorate cellulite in the skin biology or dermatology art outside of its disclosure in the above-captioned application. The use of PPARgamma stabilizers, and, more particularly, perilla oil, in the treatment or amelioration of cellulite is new and not obvious to me.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.



Dr. Peter M. Elias



date